

What is claimed is:

1. A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising the use of a first compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors and wherein said compound is administered to a patient in a dose ranging between 5 and 15 mg of the active ingredient.
2. The method of claim 1 wherein said first compound is PIPAMPERONE.
- 10 3. The method of claim 2 wherein said disease or disorder is selected from the group consisting of anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.
- 15 4. The method according to claim 1 wherein a second compound is administered simultaneously with, separate from or sequential to the first compound as defined in claim 1 to augment the therapeutic effect of said second compound.
- 20 5. The method according to claim 1 wherein a second compound is administered simultaneously with, separate from or sequential to the first compound as defined in claim 1 to provide a faster onset of the therapeutic effect of said second compound.
- 25 6. The method of claim 4 wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.
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7. The method of claim 4 wherein the first compound is administered daily at least one day before administering said second compound.
8. The method of claim 4, wherein said second compound is a selective serotonin re-uptake inhibitor.
9. The method of claim 8 wherein said selective serotonin re-uptake inhibitor is selected from the 5 group consisting of CITALOPRAM, fluoxetine, venlafaxine, fluvoxamine, paroxetine, sertraline, milnacipran, duloxetine, a pro-drug or an active metabolite thereof, and a pharmaceutically acceptable salt thereof.
10. The method of claim 9 wherein said serotonin re-uptake inhibitor is CITALOPRAM and is administered in a dose ranging between 10 and 40 mg of the active ingredient.
11. A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising the use of a composition comprising a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors.
12. The method of claim 11 wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse 20 control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.
13. The method of claim 11 wherein said first compound is selected from the group consisting of 25 PIPAMPERONE, FANANSERIN, L-745,870, PNU-101387G and U-101387 and wherein said second compound is selected from the group consisting of PIPAMPERONE, FANANSERIN, ORG 5222, ZOTEPINE, OLANZEPINE, CLOZAPINE, S16924, S18327, AMPEROZIDE, SERTINDOLE, MDL 100.907, TIOSPIRONE, FLUSPIRILENE, OCAPERIDONE, RISPERIDONE, ZIPRASIDONE, a pro-drug or an active metabolite thereof, and a pharmaceutically acceptable salt thereof.
14. The method of claim 11 wherein said composition is administered to a patient in a dose ranging between 0.5 µg and 300 mg for each of the active ingredients.

15. The method of claim 11 wherein said composition is administered simultaneously with, separate from or sequential to a third compound to augment the therapeutic effect of said third compound.
16. The method of claim 12 wherein said composition is administered simultaneously with, separate from or sequential to a third compound to provide a faster onset of the therapeutic effect of said third compound.
- 5 17. The method of claim 15 wherein said third compound is a selective serotonin re-uptake inhibitor.
18. The method of claim 17 wherein said selective serotonin re-uptake inhibitor is selected from the group consisting of CITALOPRAM, fluoxetine, venlafaxine, fluvoxamine, paroxetine, sertraline, milnacipran, duloxetine, a pro-drug or an active metabolite thereof, and a pharmaceutically acceptable salt thereof.
- 10 19. The method of claim 18 wherein said serotonin re-uptake inhibitor is CITALOPRAM and is administered in a dose ranging between 10 and 40 mg of the active ingredient.
20. A method for treating a disease or disorder as defined in claim 12 with an underlying dysregulation of emotional functionality comprising the use of a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors or of a composition comprising a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, characterized in that said compound or composition is administered simultaneously with, separate from or sequential to a nor-epinephrine re-uptake inhibitor to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor.
- 15 21. A method for treating a disease or disorder as defined in claim 12 with an underlying dysregulation of emotional functionality comprising the use of a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors or of a composition comprising a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, characterized in that said compound or composition is administered simultaneously with, separate from or sequential to a nor-epinephrine re-uptake inhibitor to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor.
- 25 22. A method for treating a disease or disorder as defined in claim 12 with an underlying dysregulation of emotional functionality comprising the use of a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors or of a composition comprising a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, characterized in that said compound or composition is administered simultaneously with, separate from or sequential to a nor-epinephrine re-uptake inhibitor to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor.
- 30 23. A method for treating a disease or disorder as defined in claim 12 with an underlying dysregulation of emotional functionality comprising the use of a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors or of a composition comprising a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, characterized in that said compound or composition is administered simultaneously with, separate from or sequential to a nor-epinephrine re-uptake inhibitor to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor.

than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, characterized in that said compound or composition is administered simultaneously with, separate from or sequential to a nor-epinephrine re-uptake inhibitor

5 to provide a faster onset of the therapeutic effect of said nor-epinephrine re-uptake inhibitor.

22. The method according to claim 20 wherein said nor-epinephrine re-uptake inhibitor is selected from the group consisting of tandamine, pirandamine, ciclazindol, fluparoxan, lortalamine, talsupram, talopram, prindamine, nomifensine, viloxazine, tomoxetine, duloxetine, venlafaxine, milnacipran, reboxetine, a pro-drug or an active metabolite thereof, and a pharmaceutically acceptable salt thereof.

10 23. A method for treating a disease or disorder as defined in claim 12 with an underlying dysregulation of emotional functionality comprising the use of a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8

15 towards other 5HT receptors or of a composition comprising a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, characterized in that said compound or composition is

20 administered simultaneously with, separate from or sequential to a neuroleptic agent to augment the therapeutic effect of said neuroleptic agent.

24. A method for treating a disease or disorder as defined in claim 12 with an underlying dysregulation of emotional functionality comprising the use of a first compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8

25 towards other 5HT receptors or of a composition comprising a first compound having (i) a selective affinity for the D4 receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, characterized in that said compound or composition is

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administered simultaneously with, separate from or sequential to a neuroleptic agent to provide a faster onset of the therapeutic effect of said neuroleptic agent.

25. The method according to claim 23 wherein said neuroleptic agent is selected from the group consisting of chlorpromazine, haloperidol, perphenazine, thioridazine, mesoridazine, trifluoperazine,

5 fluphenazine, clozapine, olanzapine, risperidone, ziprasidone, quetiapine, sertindole, aripiprazole, sonepiprazole, blonanserin, iloperidone, perospirone, raclopride, zotepine, DU-127090, ORG-5222, SM-13496, amisulpride, CP-361428, Lu 35-138, balaperidone, S-18327, WAY-135452, eplivanserin, E-5842, SR-31742, NE-100, osanetant, SR-141716, SR-48692, BSF-201640, BSF-190555, LAX-101a, sarizotan, CX-691, SB-271046, a pro-drug or active metabolite thereof, and a pharmaceutically acceptable salt thereof.

26. A method for treating a muscoskeletal disease or disorder comprising the use of a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A

15 receptor and less than 8 towards other 5HT receptors or of a composition as defined in claim 11, characterized in that said compound or composition is administered simultaneously with, separate from or sequential to a COX-2 inhibitor to augment the therapeutic effect of said COX-2 inhibitor.

27. A method for treating a muscoskeletal disease or disorder comprising the use of a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A

20 receptor and less than 8 towards other 5HT receptors or of a composition as defined in claim 11, characterized in that said compound or composition is administered simultaneously with, separate from or sequential to a COX-2 inhibitor to provide a faster onset of the therapeutic effect of said COX-25 inhibitor.

28. The method of claim 26 wherein said disease or disorder is selected from the group consisting of rheumatoid arthritis, osteoarthritis or ankylosing spondylitis.

29. The method of claim 26 wherein said COX-2 inhibitor is selected from the group consisting of celecoxib, rofecoxib, meloxicam, piroxicam, deracoxib, parecoxib, valdecoxib, etoricoxib, a chromene

30 derivative, a chroman derivative, N-(2-cyclohexyloxynitrophenyl)methane sulfonamide, COX189, ABT963, JTE-522, a pro-drug or active metabolite thereof, and a pharmaceutically acceptable salt thereof.

30. A method for preparing a compound having a selective D4 and 5-HT2A antagonist, reverse agonist or partial agonist activity comprising the following steps: (a) measuring the selective affinity of a test compound to the D4 receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the D4 receptor in respect to all the other D receptors, and measuring the
5 selective efficacy of the selected compound to the D4 receptor and selecting a compounds which is a selective antagonist, inverse agonist or partial agonist of the D4 receptor; (b) measuring the selective affinity of a test compound to the 5-HT2A receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the 5-HT2A receptor in respect to all the other 5HT receptors, and measuring the selective efficacy of the selected compound to the 5-HT2A receptor and selecting a
10 compounds which is a selective antagonist, inverse agonist or partial agonist of the 5-HT2A receptor; (c) identifying a compound which is selected in (a) and (b), (d) preparing the compound identified in (c).

31. Compound prepared by the method of claim 30.